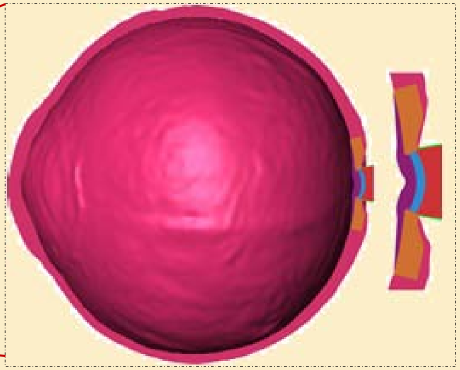
# MODELS OF THE EYE: RELEVANCE TO MICROGRAVITY INDUCED VISUAL IMPAIRMENT AND INTRACRANIAL PRESSURE



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**Human Space Endeavours Virtual Forum: The Next 50 Years**

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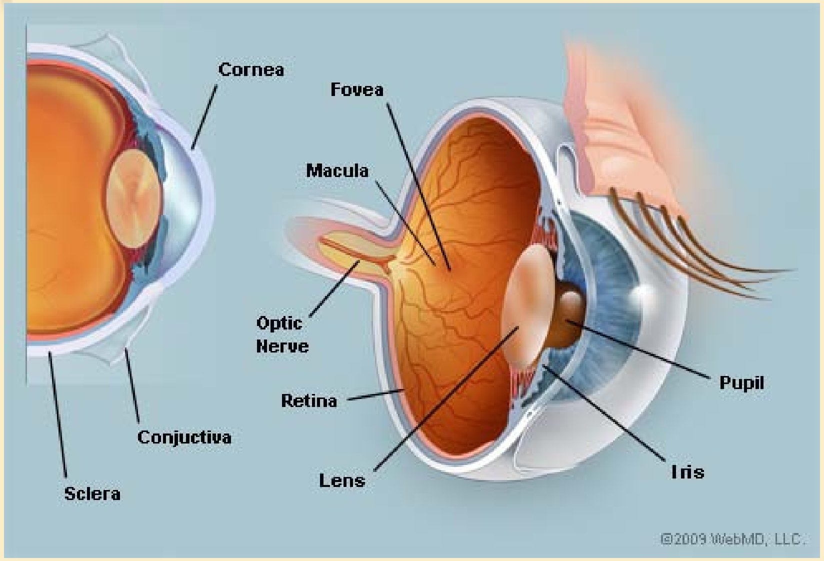
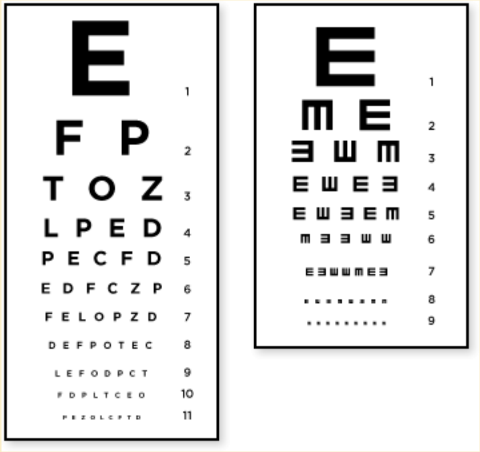
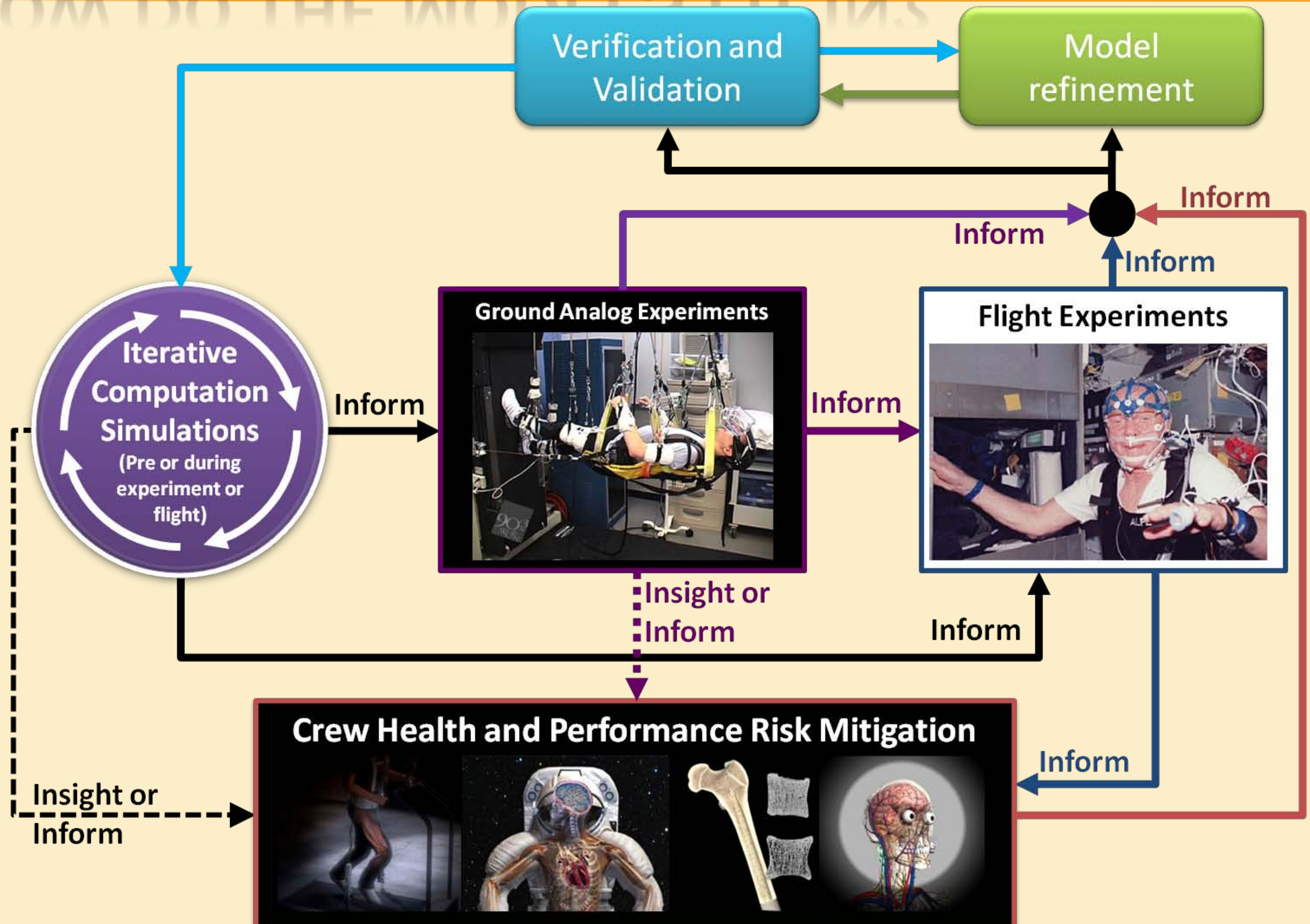
# IMPORTANCE OF MODELS IN STUDYING THE EYE

- Allows for a deeper understanding of the eye
  - How Intraocular Pressure (IOP) and mechanical property changes affect stress/strain in the eye
- Allow for possible prediction of outcomes in astronauts based on eye health



# HOW DO THE MODELS FIT IN?



# GAPS TO BE ADDRESSED

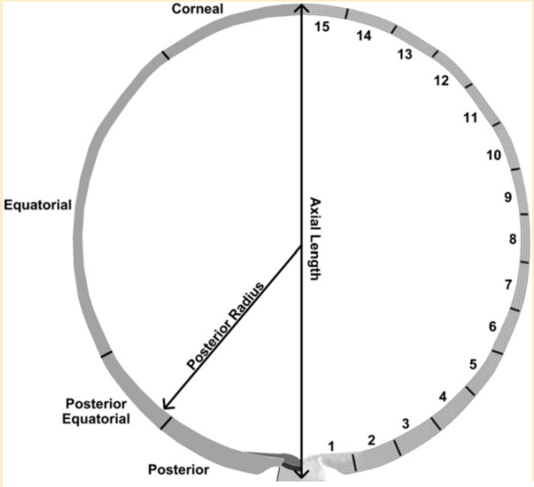
- **Gap (VIIP2)** Does exposure to microgravity cause changes in visual acuity, intraocular pressure and/or intracranial pressure? Are the effects related to mission duration?
- **Gap (VIIP4)** Are changes in visual acuity related to changes in chronic choroidal engorgement, elevated intraocular pressure and/or intracranial pressure?

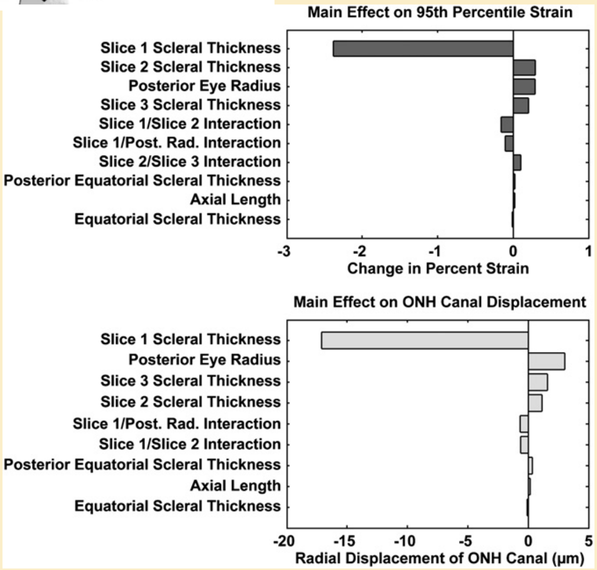
# THREE PAPERS

- Finite element modeling of the human sclera: Influence on optic nerve head biomechanics and connections with glaucoma
- The optic nerve head as a biomechanical structure: initial finite element modeling
- Factors Influencing Optic Nerve Head Biomechanics

# FINITE ELEMENT MODELING OF THE HUMAN SCLERA

- Individual specific corneoscleral shell parameters paired with idealized ONH
  - P1 – 2.4-4.6
  - P2 – 1.6-3.2
  - P3 – -3.8 - -7.3
- Sensitivity analysis conducted using idealized scleral and ONH



# THE OPTIC NERVE HEAD AS A BIOMECHANICAL STRUCTURE: INITIAL FINITE ELEMENT MODELING

- Thirteen digital 3D geometries representing idealized human eyes were studied
- Models were varied in scleral wall thickness, scleral canal shape, and inner radius
- Measured stress at 15 mm Hg IOP

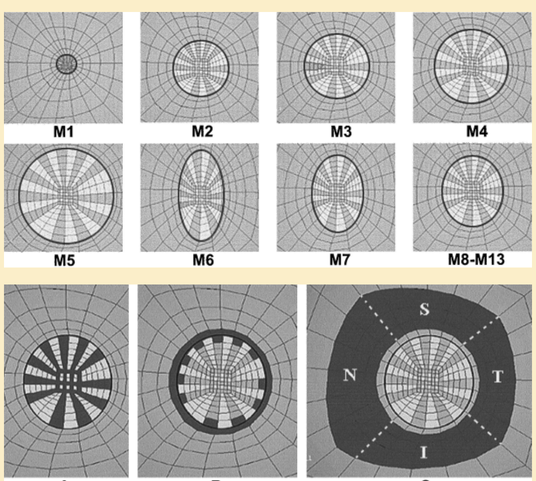


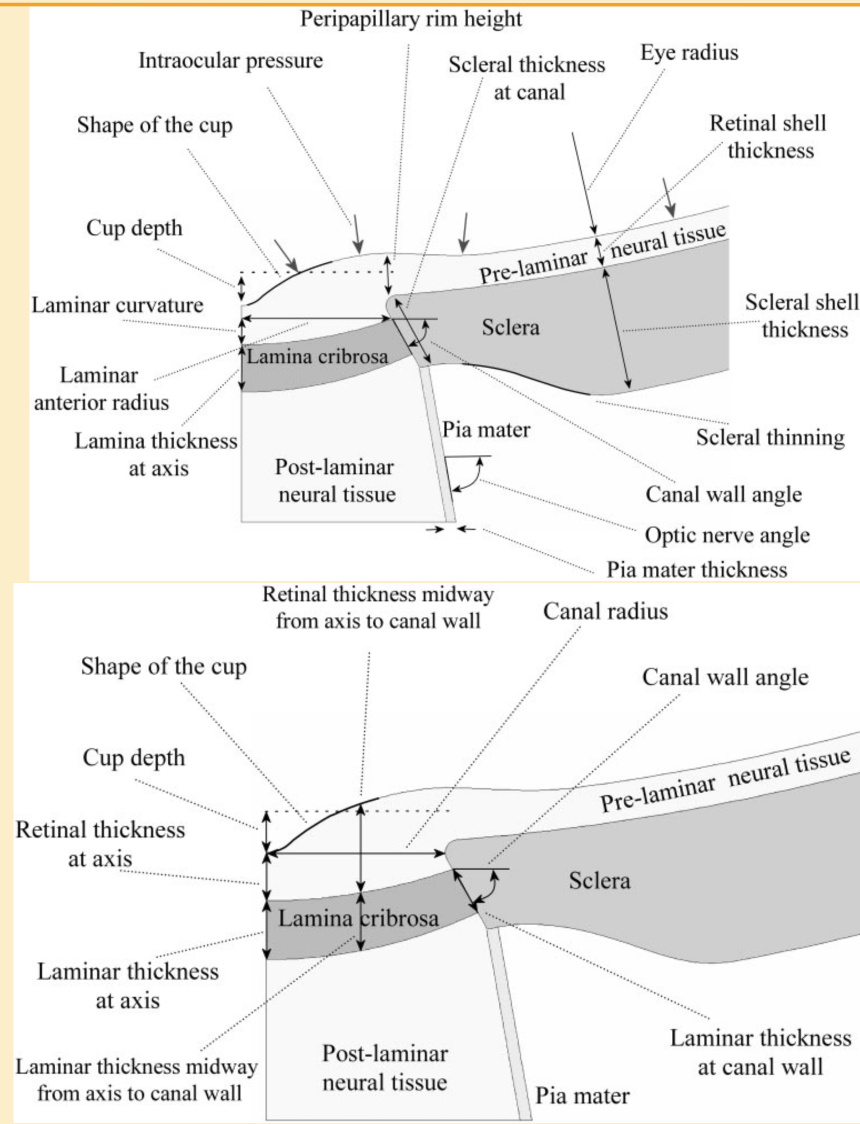

TABLE 3. Summary of the Maximum Stress Levels Expressed as Multiples of IOP

| Model | Posterior Sclera | Peripapillary Sclera | Laminar Insertion Zone | Laminar Trabeculae |
|---|---|---|---|---|
| Circular | | | | |
| M1 (0.50 × 0.50) | 11 | 11 | 20 | 34 |
| M2 (1.50 × 1.50) | 11 | 15 | 31 | 54 |
| M3 (1.75 × 1.75) | 11 | 16 | 34 | 65 |
| M4 (2.00 × 2.00) | 11 | 17 | 38 | 77 |
| M5 (2.56 × 2.56) | 11 | 20 | 47 | 107 |
| Elliptical | | | | |
| M6 (2.50 × 1.25) | 11 | 21 | 40 | 72 |
| M7 (2.10 × 1.40) | 11 | 17 | 35 | 65 |
| M8 (1.92 × 1.67) | 11 | 16 | 35 | 67 |
| Wall thickness | | | | |
| M9 (0.5) | 17 | 27 | 63 | 122 |
| M8 (0.8) | 11 | 16 | 35 | 67 |
| M10 (1.0) | 9 | 13 | 27 | 50 |
| M11 (1.5) | 6 | 8 | 16 | 28 |
| Inner radius | | | | |
| M8 (12.0) | 11 | 16 | 35 | 67 |
| M12 (13.0) | 12 | 17 | 36 | 66 |
| M13 (14.0) | 13 | 18 | 38 | 66 |

All dimensions shown in millimeters. Data are the means of the highest 5% of stress magnitude values (from Table 2) expressed as multiples of IOP.

# FACTORS INFLUENCING OPTIC NERVE HEAD BIOMECHANICS

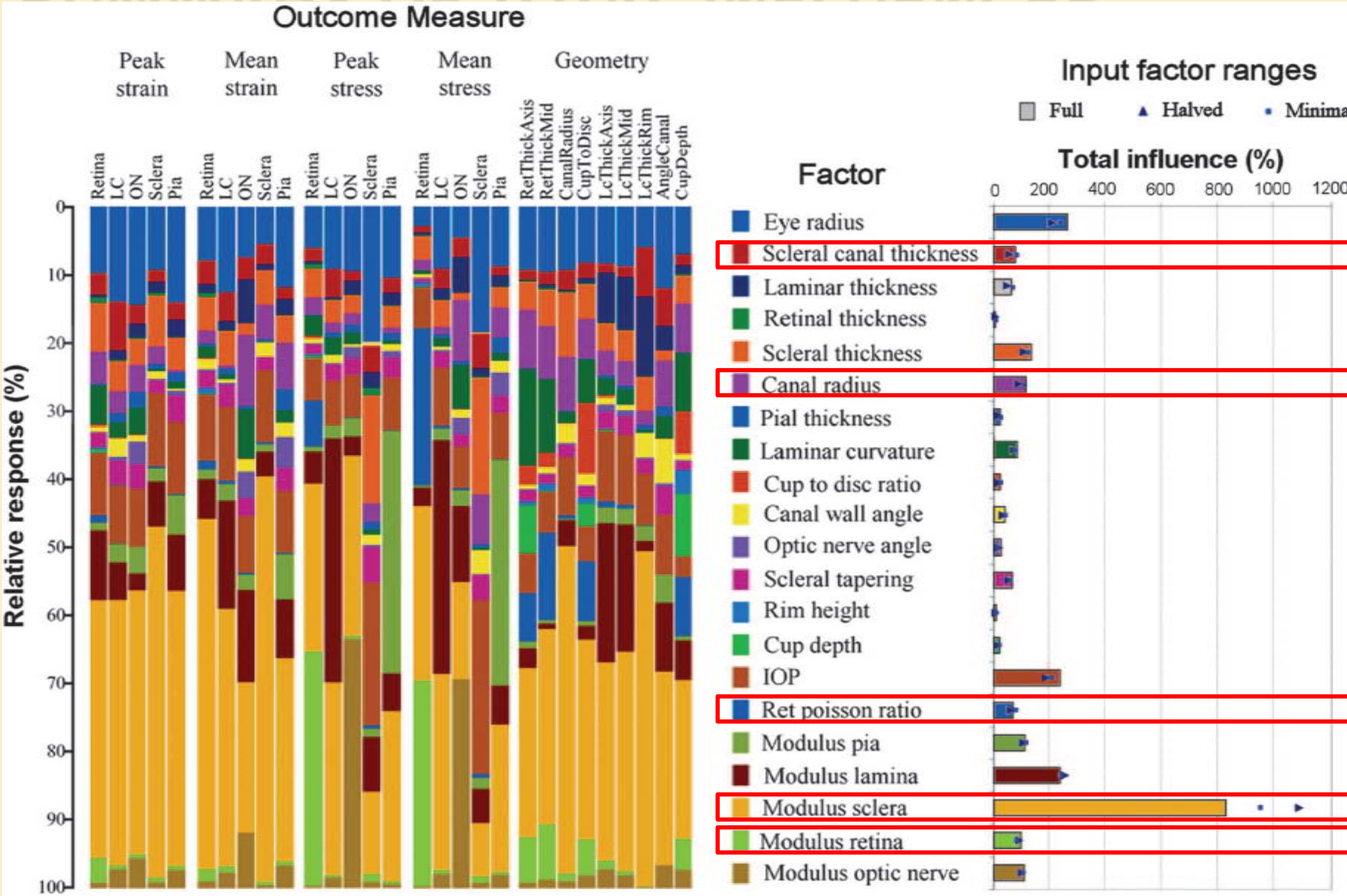
- Detailed sensitivity analysis of ONH to various input factors
- Measured outcomes via different output factors



# METHOD OF COMPARISON BETWEEN INPUT FACTORS

- Absolute response - the range of outcomes by varying only one input factor of a particular outcome
- Total response - the sum of the absolute responses for one particular outcome
- Relative response - absolute response of one factor divided by the total response
- Total influence – sum of relative responses of single input over all outcomes

# SUMMARY OF TOTAL INFLUENCES



# OTHER IMPORTANT INFORMATION

**Table 1.** Histomorphometric Measurements of the Lamina Cribrosa

| | Control Group | Glaucoma Group | P |
|---|---|---|---|
| n | 42 | 11 | |
| Lamina cribrosa thickness (μm) | | | |
| Central region | 457.7 ± 163.7 | 201.5 ± 251.5 | <0.001 |
| Median | 464.0 | 75 | |
| Range | 92–1008 | 39–868 | |
| Midperipheral region | 463.3 ± 167.6 | 173.3 ± 191.2 | <0.001 |
| Median | 441.5 | 62 | |
| Range | 133–1013 | 30–684 | |
| Midperipheral region | 461.3 ± 189.6 | 188.9 ± 241.3 | <0.001 |
| Median | 441.0 | 84 | |
| Range | 111–1353 | 28–850 | |
| Peripheral region | 435.3 ± 130.6 | 161.4 ± 184.2 | <0.001 |
| Median | 447.0 | 99 | |
| Range | 82–714 | 38–658 | |
| Peripheral region | 464.9 ± 190.6 | 162.6 ± 194.1 | <0.001 |
| Median | 457.5 | 60 | |
| Range | 71–1290 | 33–663 | |
| Ratio of inner to outer lamina cribrosa surface | 0.88 ± 0.12 | 0.99 ± 0.05 | 0.002 |
| Median | 0.87 | 1.0 | |
| Range | 0.57–1.35 | 0.85–1.0 | |
| Length of the posterior surface of the lamina cribrosa directly exposed to the pia mater and indirectly to the cerebrospinal fluid space (μm) | 39.4 ± 99.6 | 310.2 ± 299.0 | <0.001 |
| Median | 0 | 321 | |
| Range | 0–334 | 0–842 | |
| Shortest distance (μm) between inner surface of the lamina cribrosa and cerebrospinal fluid space | 847.0 ± 224.8 | 606.9 ± 382.3 | <0.001 |
| Median | 810.5 | 511 | |
| Range | 384–1488 | 307–1710 | |
| Shortest distance (μm) between inner surface of the lamina cribrosa and inner surface of the pia mater | 557.9 ± 172.1 | 335.4 ± 266.6 | <0.001 |
| Median | 546.0 | 314 | |
| Range | 185–998 | 99–1079 | |

Data are expressed as the mean ± SD. *P* is the significance of the differences (Mann-Whitney test) between the two study groups.

Relative Distances b/t structures in the eye - “Anatomic Relationship between Lamina Cribrosa, Intraocular Space, and Cerebrospinal fluid Space” – Jonas et al.

**Table 1.** Summary of Mechanical Properties of ONH Tissues

| Tissue/Species | Author(s) | Young's Modulus (MPa) |
|---|---|---|
| Sclera | | |
| Tree Shrew | Phillips and McBrien[23] | 2.28 |
| Tree Shrew | Siegwart and Norton[24] | 0.69–18.3 |
| Bovine | Smolek[25] | 3.8–9.0 |
| Human | Woo et al.[26] | 5.5 |
| Human | Friberg and Lace[27] | 1.8–2.9 |
| Monkey | Downs et al.[28] | 2.9–5.5 |
| Porcine | Spörl E, et al. *IOVS* 2003;44:ARVO E-Abstract 3318 | 0.3 |
| Human | Battaglioli and Kamm[29] | 4.76 |
| Human | Kobayashi et al.[30] | 5.5 |
| Neural tissue | | |
| Porcine brain | Miller[31] | 0.03 |
| Bovine brain | Guillaume et al.[32] | 0.046 |
| Monkey brain | Merz et al.[33] | 0.010 |
| Bovine retina | Jones et al.[34] | 0.020 |
| Cat spinal cord | Chang et al.[35] | 0.2–0.6 |
| Rabbit spinal cord | Ozawa et al.[36] | 0.035 |
| Lamina cribrosa | | |
| Porcine | Spörl E, et al. *IOVS* 2003;44:ARVO E-Abstract 3318 | 0.1 |
| Fit to human | Edwards and Good[6] | 0.14–0.38 |
| Monkey | Bellezza et al.[37] | 0.077–0.405 |
| Pia mater | | |
| Human | Zhivoderov et al.*[38] | 1.44–4.65 |
| Human | Our computations based on measurements by Mazuchowski and Thibault[39] | 2.5–65 |
| Human | Brands[40] | 1.86 (Shear modulus) |

The Young's moduli chosen for this study were: sclera, 3 MPa; lamina cribrosa, 0.3 MPa; neural tissue, 0.03 MPa; pia mater, 3 MPa; and central retinal vessels, 0.3 MPa. Results of a parametric study based on these values are shown in Figure 7.

* As cited by Kleiven.[41]

Mechanical Properties of the human eye “Finite Element Modeling of Optic Nerve Head Biomechanics” – Sigal et al.

# MORE MATERIALS PROPERTIES

TABLE 1. Input Factors and Their Baseline Values and Ranges Used in the Sensitivity Analysis (see Figure 1 for Factor Definitions)

| Name | Coded Name | Units | Baseline | Low | High | Sources |
|---|---|---|---|---|---|---|
| Input factors defining the geometry of the eye and ONH | | | | | | |
| Internal radius of eye shell | EyeRadius | mm | 12.0 | 9.6 | 14.4 | 9–13 |
| Scleral thickness at canal | ScThickAtCanal | mm | 0.4 | 0.32 | 0.48 | 13–16 |
| Laminar thickness at axis | LCThickAxis | mm | 0.3 | 0.24 | 0.36 | 13,16–18 |
| Retinal thickness | RetThickShell | mm | 0.2 | 0.16 | 0.24 | 19,20 |
| Scleral shell thickness | ScThickShell | mm | 0.8 | 0.64 | 0.96 | 11,14,15 |
| LC anterior surface radius | LCRadius | mm | 0.95 | 0.76 | 1.14 | 10,12,13,16,18,21–24 |
| Pia mater thickness | PiaThick | mm | 0.06 | 0.048 | 0.072 | 13 |
| Laminar curvature | LCDepth | mm | 0.2 | 0 | 0.2 | * |
| Cup-to-disc ratio/shape of the cup | Cup2DiscRatio | — | 0.25 | 0.1 | 0.5 | 19,21 |
| Canal wall angle to the horizontal | AngleScCanal | deg | 60 | 48 | 72 | * |
| Optic nerve angle | AngleON | deg | 80 | 64 | 96 | * |
| Scleral thinning/peripapillary scleral tapering | ScThinFactor | — | 0.5 | 0 | 1.0 | 11,15 |
| Peripapillary rim height | RimHeight | mm | 0.3 | 0.24 | 0.36 | 19,21,25 |
| Cup depth | CupDepth | mm | 0.33 | 0.26 | 0.4 | 19,21 |
| Input factors defining the load on ONH tissues | | | | | | |
| Intraocular pressure | IOP | mm Hg | 25 | 20 | 30 | 26,27 |
| Input factors defining the biomechanical properties of relevant optic tissues | | | | | | |
| Poisson ratio of retina | RetPoisson | — | 0.49 | 0.4 | 0.49 | 28–30 |
| Pia mater Young's modulus | PiaModulus | MPa | 3 | 1 | 9 | 31–33 |
| Lamina cribrosa Young's modulus | LCModulus | MPa | 0.3 | 0.1 | 0.9 | 6,34–36 |
| Sclera Young's modulus | ScModulus | MPa | 3 | 1 | 9 | 29,37–44,54 |
| Retina Young's modulus | RetModulus | MPa | 0.03 | 0.01 | 0.09 | 45–50 |
| Optic nerve Young's modulus | ONModulus | MPa | 0.03 | 0.01 | 0.09 | Same as for retina |

Ranges were estimated from our own measurements (*), or from a combination of our measurements and the sources listed (see the Methods section for details). In many cases, the sources did not directly measure the quantity of interest. In such situations, we computed the quantity of interest from the data that were reported.

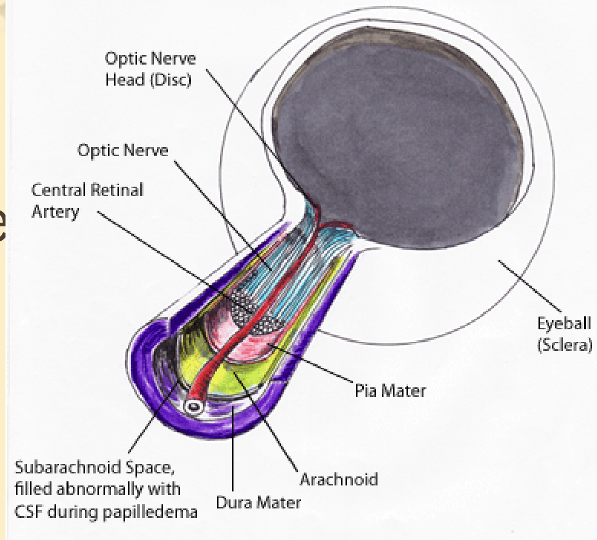
Mechanical Properties of the human eye
"Factors Influencing Optic Nerve Head
Biomechanics– Sigal et al.

# ASSUMPTIONS AND CONSIDERATIONS

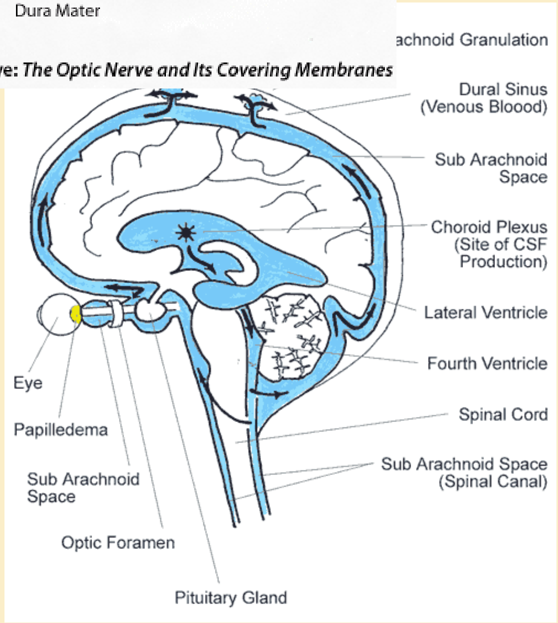
- Several simplifications
  - Geometries
  - Linear materials properties
  - Ignores some important aspects of structure, such as the non-homogeneity nature of the various tissues
- Future work needed
  - Obtain non-linear materials properties
  - Account for non-homogeneity in structures
  - Make shapes of the eye more realistic

# CONNECTION WITH THE BRAIN AND ICP

- CSF acts on optic nerve of eye
  - Compress nerve and vasculature
  - Push against lamina cribrosa
- Effects on ON not understood
- Pressure against LC causes deformation and can disrupt trans-laminar pressure
- Possibility of segregation of CSF due to increased ICP




Posterior View of Eye: *The Optic Nerve and Its Covering Membranes*

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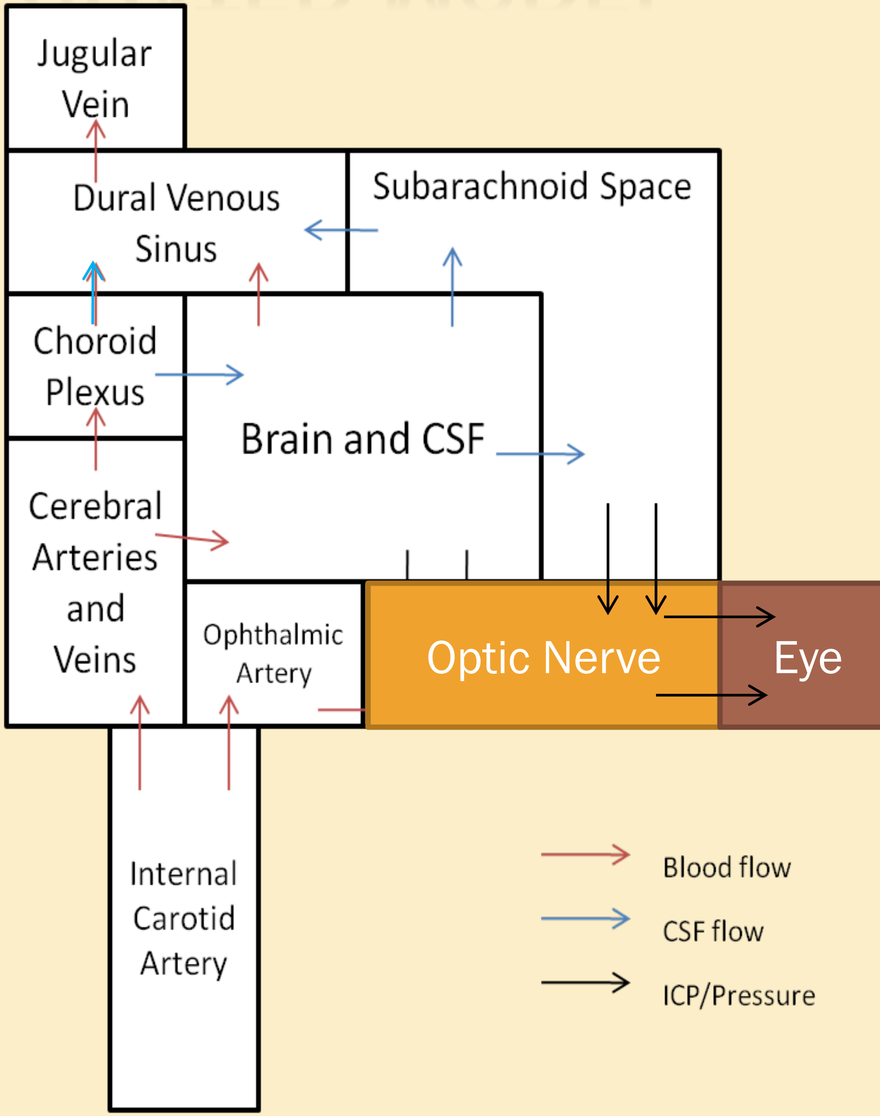
# RECOMMENDATIONS

- For design of the model
  - Begin with the current linear materials properties currently in literature → good starting point
  - Use an idealized geometry
  - Integrate eye model with brain/CSF as single model or through inputs/outputs
- Once a simplified model is created
  - Account for realistic structure of the eye → Jonas et al.
  - Find or measure non-linear viscoelastic properties

# PRELIMINARY VIIP INTEGRATED MODEL

- Based on 7-compartment model proposed by Sorek et al.
- Accounts for interactions between vascular and cerebral fluid systems



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